

## REMARKS

## A. Status of the Claims

The Nonfinal Office Action mailed January 5, 2007 rejoined Groups I and II from the Restriction Requirement of October 11, 2006, and withdrew claims 19-36 from further consideration as being drawn to a nonelected invention. The resulting status of the claims at this time therefore is that claims 1-18 are pending, and claims 19-36 are withdrawn.

## B. Restriction Requirement

Applicant gratefully acknowledges rejoinder of Groups I and II of the Restriction Requirement mailed October 11, 2006.

Applicant respectfully points out that claims 25-34 recite methods of use for the specificity-determining substrate recited in claim 1 of Group I. Therefore upon a finding of allowability of claim 1, Applicant respectfully requests rejoinder and examination of claims 25-34 in the proceedings of the instant application.

Applicant further confirms the following elections of species:

- a) succinyl as the specificity determining ligand in claims 2 and 11, and
- b) silica as the support in claims 5 and 14.

Applicant has amended claims 1 and 4 in such a way as to delete recitation of particular species of spacer. Therefore Applicant believes that an election of a species of spacer is no longer necessary (see also Section D below).

Applicant reserves the right to prosecute the subject matter of all nonelected inventions in subsequent patent applications.

## C. Communication mailed September 21, 2007.

The Communication mailed September 21, 2007 requests that a listing of all claims readable on a “silica surface” as the elected support, on the “succinyl group” as the elected specificity-determining ligand, and of an elected spacer be provided.

Applicant believes that the following listing of claims fulfils the above request:

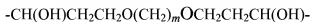
- a) Claims readable on a “silica surface”: Claims 1, 5, 6, 7, 10, 14, 15, and 16.
- b) Claims readable on the “succinyl group” as the elected specificity-determining ligand:

Claims 1, 2, 10, and 11.

D. Communication mailed December 31, 2007.

The communication mailed December 31, 2007 reiterates the requirement to elect a single particular structure of spacer, specified as to atom and bond from which the search will commence.

Applicant respectfully provisionally elects **with traverse** the spacer



from which the search will commence. This provisional election with traverse of species of spacer reads on no currently recited claim, but may relate to disclosure supporting claim 4 as amended. Since no “spacer” is recited in claim 1 as amended, this election does not read on claim 1.

Applicant respectfully traverses the requirement for election of species of spacer, since claim 4 as currently amended does not recite any species of spacer. The following traverse responds to the substance of an informal telephonic discussion with Examiner Christopher Gross held on January 4, 2008 concerning this requirement.

Applicant believes restriction requirements must be based on **claimed** species, whereas this restriction requirement is improperly based on restricting **disclosed** species.

The statute at 35 U.S.C. 121 states in relevant part:

“If two or more independent and distinct inventions are **claimed** in one application, the Director may require the application to be restricted to one of the inventions....” (emphasis added).

The statute establishes authority for promulgating rules for its implementation at 35 U.S.C. 2 (b) (2) (A):

“The Office... may establish **regulations**, not inconsistent with law, which...shall **govern the conduct of proceedings in the Office.**”

Of relevance to the present argument USPTO Rule 37 CFR 1.142(a) states in relevant part, in implementing 35 U.S.C. 121:

“If two or more independent and distinct inventions are **claimed** in a single application, the examiner in an Office action will require the applicant in the reply to that action to elect an invention to which the claims will be restricted...” (emphasis added).

The Introduction to the MPEP as available at [www.uspto.gov](http://www.uspto.gov) (8<sup>th</sup> ed., revised September 2007) states:

“The primary function of the rules is to advise the public of the rules which have been established **in accordance with the statutes** and which **must be followed before the USPTO. The rules govern the examiners**, as well as applicants and their attorneys and agents.” (emphasis added).

In distinction to the statute and regulations quoted above, MPEP 809.02(a) states, apparently inappropriately, in relevant part:

“Applicant should then be required to elect a single **disclosed** species under 35 U.S.C. 121...” (emphasis added).

Since the statute and the rule are clearly in conflict with the MPEP, it is the **statute** as embodied in 35 U.S.C. 121 and the **rule** as embodied in 37 CFR 1.142(a) that prevails over the MPEP. The MPEP has no force of law, whereas the statute **is** the law and the rule **implements** the law by statute. When administrative guidelines such as the MPEP conflict with statute and/or with a rule of the Code of Federal Regulations, actions taken **must conform** to the statute and the rule and **not** to the MPEP.

In conformance with 35 U.S.C. 121 and Rule 37 CFR 1.142(a) Applicant respectfully requests withdrawal of the requirement for restriction of species of spacer as improperly requiring election among **disclosed** but not **claimed** species, and requests that claim 4 be examined as currently amended. Applicant reserves the right to petition for withdrawal of this restriction requirement in the event this request is denied..

#### E. Amendments to the Claims

The amendment to claim 1 reciting “suitable for proteomic separations” is supported throughout the specification, and in particular at least at page 1, in the section Field of the Invention; page 3, 2<sup>nd</sup> paragraph; and page 11, 5<sup>th</sup> paragraph of text.

The amendments to claims 1 and 10 related to forming a reversible complex are supported at least at page 6, paragraph 3; at page 16, 4<sup>th</sup> paragraph, and in the Examples.

The amendment to claim 1 reciting “wherein the predetermined minimum distance is greater than about 5 Å” is supported in the specification at least at page 12, 3<sup>rd</sup> paragraph.

No new matter is introduced in the amendments to the claims.

## ARGUMENT

A. Claims 1-18 are patentable under 35 U.S.C. 112, 2<sup>nd</sup> paragraph.

The Office Action cites the word “predetermined” as lacking a clear definition in the specification. As part of this rejection the Office Action erroneously states that paragraph 0081 of the specification provides numbers such as “4” for the minimum distance, but that no units are given (page 3, 7<sup>th</sup> paragraph of text). Applicant respectfully points out that in the specification as filed each number in the indicated paragraph is followed by the symbol “Å” (meaning Angstrom units, or 0.1 nm). The same symbols “Å” appear on the USPTO web site providing the electronic version of Published Patent Application 20040106131 for this application in the TIFF image pages. Thus the Office Action is mistaken in stating that no units are provided for the numbers. (Applicant has noted that in the html version of the same Patent Application Publication the symbols “Å” are missing; this may be the source of the error.) In view of Applicant’s perfecting of the view of the specification, Applicant declares that the meaning of “predetermined minimum distance” is provided in the specification as filed.

Nevertheless Applicant has amended claim 1 to recite that the predetermined minimum distance is greater than about 5 Å. Accordingly Applicant submits that claim 1 as amended particularly points out and distinctly claims the subject matter which Applicant regards as the invention.

The Office Action rejects claims 6 and 15 for indefiniteness in reciting “a predetermined maximum content” but lacking clear definition as to the meaning of “predetermined” in the specification. Applicant respectfully points out that the specification, at page 12, 2<sup>nd</sup> paragraph (paragraph 0080) provides an extensive definition of the phrase “predetermined maximum content”. Thus Applicant submits that claims 6 and 15 are clear, and that they particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

For these reasons Applicant respectfully submits that claims 1-18 satisfy the requirements of 35 U.S.C. 112, 2<sup>nd</sup> paragraph, and requests that this rejection be withdrawn at this time.

B. Claims 1-6, and 10-15 are novel under 35 U.S.C. 102(b) as not anticipated by Keyes (U. S. Patent 4,714,676).

The present invention provides a specificity-determining substrate suitable for proteomic separations, wherein the specificity-determining substrate includes a specificity-determining ligand bound to a support wherein the spatial separation between adjacent ligand groups is greater than a predetermined minimum distance of about 5 Å (claim 1). The specificity-determining substrate reversibly forms a complex with a protein molecule in a homogenous fashion. Thus, in this invention, a specificity-determining ligand is linked to a support. Among the specificity-determining ligands set forth in claim 2, Applicant has elected the succinyl group as the species subject to examination at this time. Thus according to claim 2, a succinyl group is covalently bound to a substrate. The specificity-determining substrate that includes the succinyl-substrate combination has the property that it forms a noncovalent complex with a protein molecule in a homogeneous fashion.

The present invention further provides a complex that includes a specificity-determining substrate as described in the preceding paragraph and a reversibly bound protein molecule (claim 10). In particular, the complex includes a reversibly bound protein molecule and a specificity-determining substrate that forms a complex with a protein molecule in a homogenous fashion. Thus, in this invention, a specificity-determining ligand that is elected as succinyl is linked to the support. Applicant emphasizes that in the complex, the specificity-determining ligand (succinyl) is bound to the support, and not to the protein moiety.

Keyes relates broadly to a naturally occurring protein that is chemically modified to provide the protein with activity of a selected enzyme (see Abstract). Keyes elaborates that a native protein is partially denatured in the presence of an inhibitor for the predetermined model enzyme, whose activity is to be modeled. Next, the partially denatured native protein, in the presence of the inhibitor of the model enzyme, is crosslinked and covalently immobilized on a solid support to define a new immobilized enzyme-like modified protein conformation which is defined by the inhibitor of the model enzyme and is preserved in an immobilized fashion on a solid carrier or support. (see Abstract and Summary of the Invention (col. 3, lines 45-46)) In an embodiment, Keyes discloses that a native protein may be reacted with succinic anhydride. Applicant emphasizes that in this reference it is the protein that is irreversibly immobilized on a support and reacted with succinic anhydride.

Accordingly Applicant points out that Keyes fails to provide a specificity-determining substrate, wherein the specificity-determining substrate includes a specificity-determining ligand

bound to a support, wherein the specificity-determining substrate reversibly forms a complex with a protein molecule that is suitable for proteomic separations, and wherein the spatial separation between adjacent ligand groups is greater than a predetermined minimum distance of about 5 Å (claim 1). Keyes further fails to provide a complex that includes a specificity-determining substrate as described in the instant invention and a reversibly bound protein molecule (claim 10). In particular, Applicant emphasizes that Keyes, in an embodiment, provides an immobilized protein reacted with succinic anhydride. Since it is immobilized, it is not reversibly bound. Further, Keyes fails to provide any protein that forms a reversible complex with the structure disclosed in the reference. On the basis of these fundamental distinctions, Keyes fails to anticipate claims 1-6, and 10-15. Accordingly, Applicant respectfully requests that this rejection be withdrawn at this time.

C. Claims 1-6, 8-15, and 17-18 are novel under 35 U.S.C. 102(b) as not anticipated by Comb et al. (U. S. Patent 5,834,247).

Comb et al. relates broadly to modified proteins comprising an intervening protein sequence (IVPS) and a target protein, the IVPS being capable of excision by protein splicing, or cleavage in the absence of splicing, under predetermined conditions. (See Summary of the Invention) Comb et al. provides numerous modalities for preparing such modified proteins using combinations of recombinant DNA techniques and protein chemistry techniques (See Summary of the Invention)

Applicant respectfully points out that Comb et al. fails to provide a specificity-determining substrate that reversibly forms a complex with a protein molecule, suitable for proteomic separations, wherein the spatial separation between adjacent ligand groups bound to a substrate is greater than a predetermined minimum distance, of about 5 Å. The Office Action cites Fig. 28 as teaching a chitin binding column for the purification of expressed proteins fused with an intein and chitin binding domain (page 5, 4<sup>th</sup> paragraph). Applicant has scrutinized Fig. 28 as well as the specification, and respectfully notes failure to find any disclosure related to Fig. 28 that refers to a chitin binding column. Furthermore, any citation of a chitin column for binding to a chitin binding domain of a multicomponent fusion protein does not provide a specificity-determining substrate that reversibly forms a complex with a native protein suitable for proteomic separations. Comb et al. employ chitin to bind a unique moiety of an artificially

fused protein, namely the binding only of a chitin binding domain (CBD) of a fusion protein. For this reason Comb et al. do not provide a column that reversibly binds a native protein suitable for proteomic separations. Thus this citation to Comb et al. in the Office Action is inapposite.

For these reasons Comb et al. does not anticipate claims 1-6, 8-15, and 17-18. Accordingly Applicant respectfully requests that this rejection be withdrawn at this time.

D. Claims 1-18 are nonobvious under 35 U.S.C. 103(a) over Comb et al. in view of Margel (U. S. Patent 4,732,811).

The Office Action has rejected claims 1-18 for obviousness over Comb et al. in view of Margel (page 6, 7<sup>th</sup> paragraph of text), even though the substance of the obviousness rejection is directed to the purported prima facie obviousness of only claims 7 and 16 (Office Action, pages 6-7).

In the absence of substantive grounds of rejection for obviousness of claims 1-6, 8-15, and 17-18, Applicant considers these claims to be nonobvious under 35 U.S.C. 103(a) on their face. Furthermore, Applicant has clearly pointed out the deficiencies of Comb et al. above. Margel fails to remedy these deficiencies. Therefore Applicant respectfully submits that claims 1-18 are patentable under 35 U.S.C. 103(a) over the prior art of record, and request that the rejection of these claims be withdrawn at this time.

Margel relates generally to agarose and agar polyaldehyde beads, and processes for the synthesis of such beads. The polyaldehyde compounds e.g. polyacrolein, polymethacrolein or polyglutaraldehyde, are used as microspheres or as powders (see Abstract).

Claims 7 and 16 are dependent claims that recite the specificity-determining substrate of the invention, or the complex of the invention, respectively, wherein the solids content of the support when equilibrated with an ambient fluid is less than about 8% w/v. It is emphasized that this recitation relates to the proportion of solids within the volume occupied by a substrate composition in equilibrium with its ambient fluid medium. This is distinct from the interpretation in the Office Action that misrepresents the recitation as being the solids content of any slurry or suspension of the specificity-determining substrate, or the complex, in a fluid such as an aqueous or buffering medium. These are not the same; a suspension clearly includes the

fluid in excess of the volume contained within the bounds of a particle. Thus Margel fails to provide the limitation recited in claims 7 and 16.

Margel does not remedy the deficiencies identified in Comb et al. with respect to independent claim 1 reciting the specificity-determining substrate of the invention, nor with respect to dependent claim 10 reciting the complex of the specificity-determining substrate with a protein. Specifically, no combination of Comb et al. with Margel provides the inventions, considered as a whole, provided in dependent claims 7 and 16. Accordingly Applicant submits that claims 7 and 16 are nonobvious under 35 U.S.C. 103(a) over the prior art of record. Applicant respectfully requests that this rejection be withdrawn at this time.

### CONCLUSION

Applicant has shown that claims 1,2, 4-11, and 13-18, currently subject to examination under the species election provided by Applicant, are patentable over all grounds of rejection presented in the Office Action. Applicant respectfully requests that these rejections be withdrawn at this time.

Upon finding that claims 1,2, 4-11, and 13-18 as currently restricted are patentable, Applicant respectfully requests that all of claims 1-18 be examined with respect to all species therein.

Respectfully submitted,

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